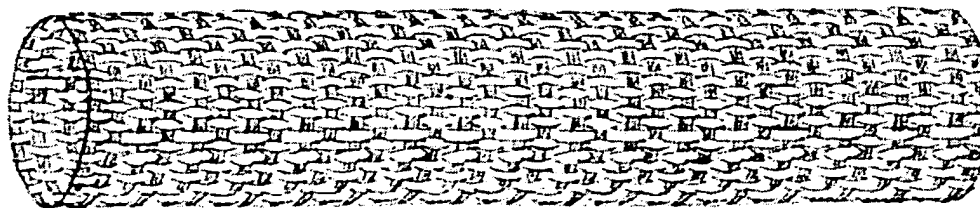


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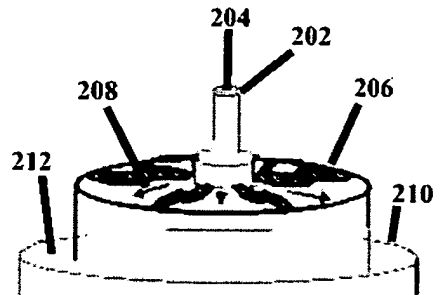
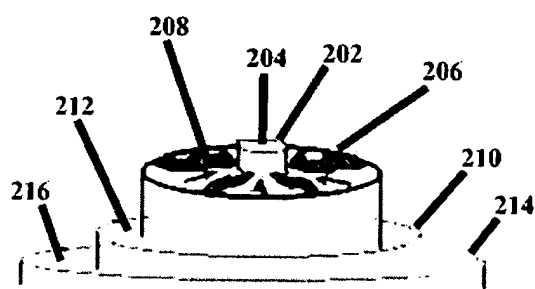
10

FIGURE 1

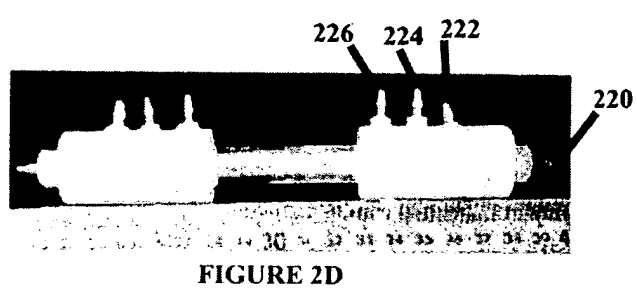
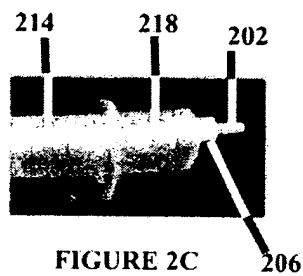
5

10

15



20



25

30

FIGURE 2

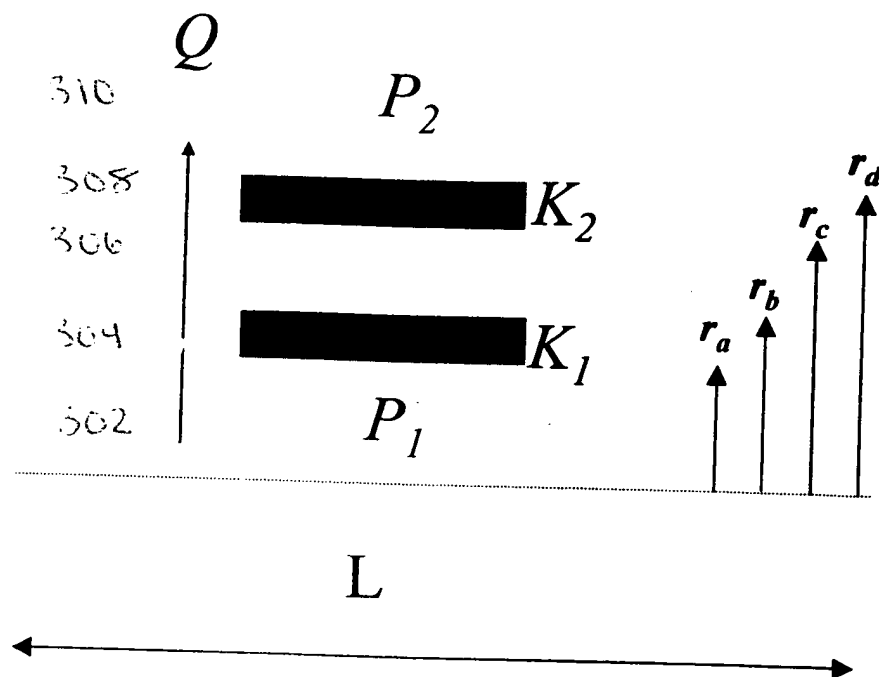


Figure 3

125th

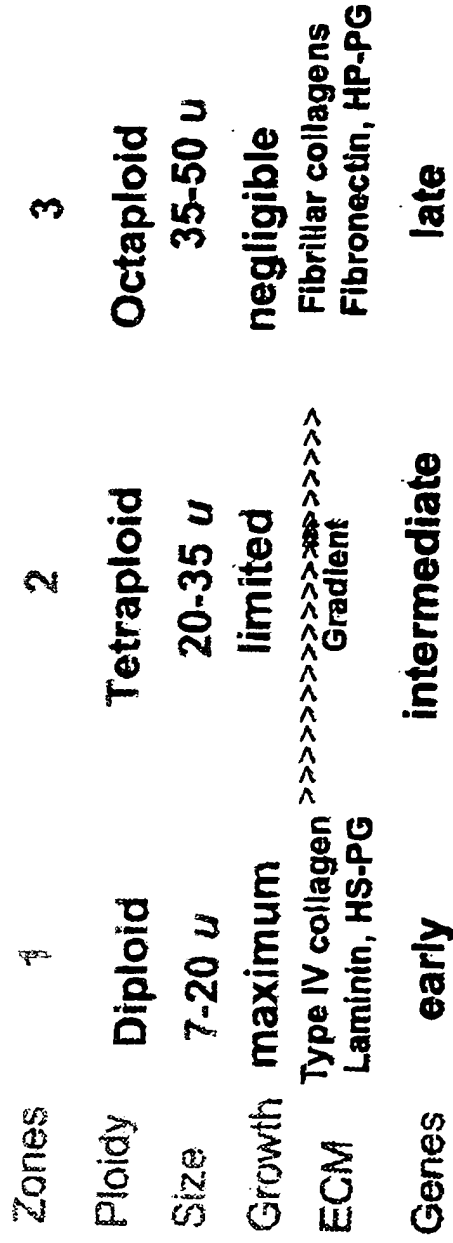
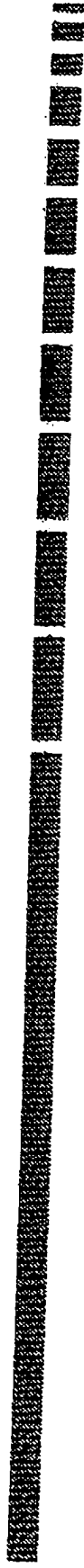


Figure 4

Multicoaxial Bioreactor Design



Liver Acinus



Coaxial Fibers

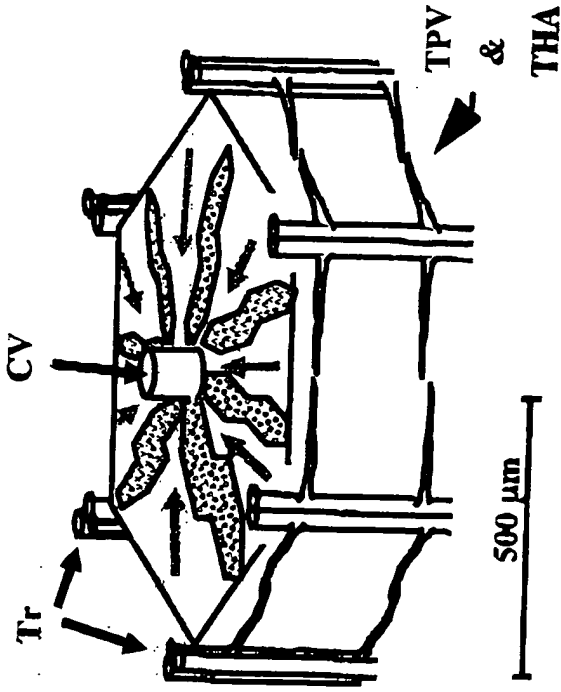
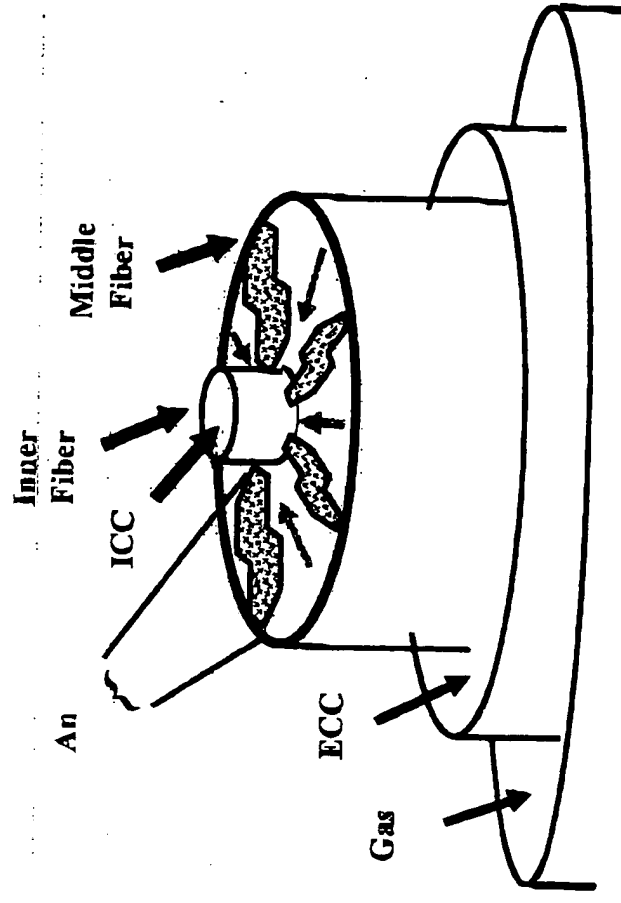
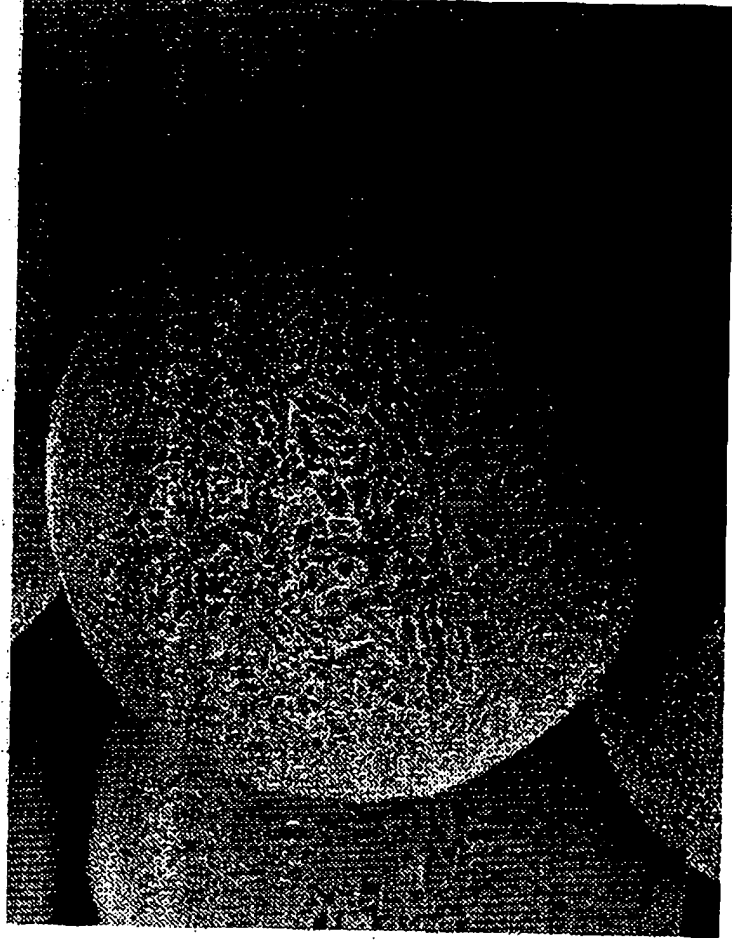


Figure 5

Porous, Biocompatible, Biodegradable PLGA Microcarriers for Cells in Bioreactors



20µm 1000X

Figure 6

Physical Analysis of the Liver

Acinus

Components of Mass Transfer:

$$\underbrace{\frac{\partial c}{\partial t}}_{\text{Gas, Nutrient or Metabolite Profile or Map}} = \underbrace{D \nabla^2 c}_{\text{Diffusion } (10^{-6} \text{ cm}^2/\text{s}, 200 \mu\text{m})} + \underbrace{v \cdot \nabla c}_{\text{Convection } (140 \cdot 10^{-2} \text{ cm/s, meters})} + \underbrace{R}_{\text{Metabolism } (0.5 \text{ nmol O}_2/\text{s}/10^6 \text{ cells})}$$

•PORTAL TRIAD

- Portal venule
- Hepatic arteriole
- Bile ductule
- Lymph vessel

CENTRAL VENULE

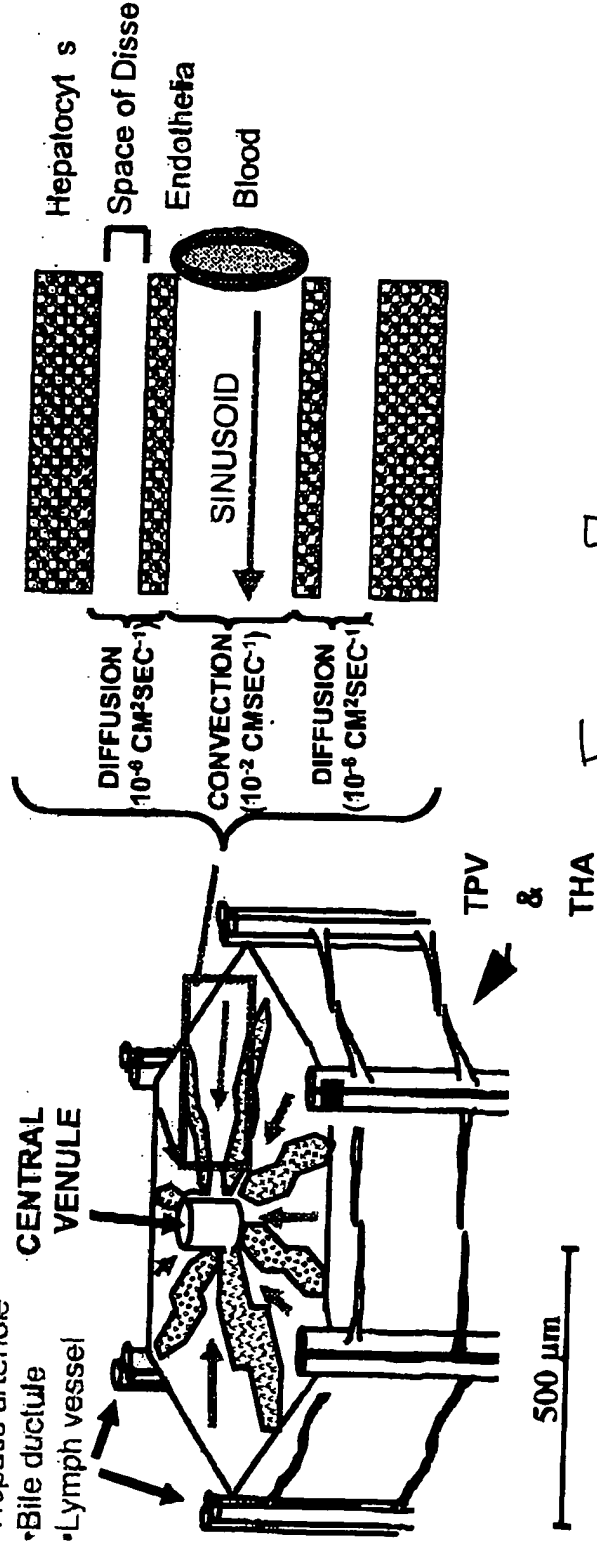
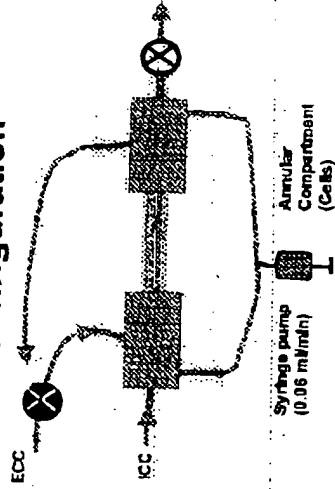


Figure 7

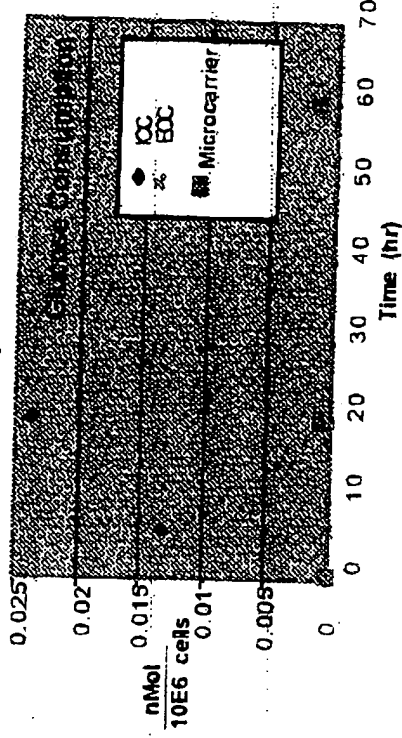
Membrane 'Fouling' Studies

CELL STUDY OF DEAD-ENDED FLOW

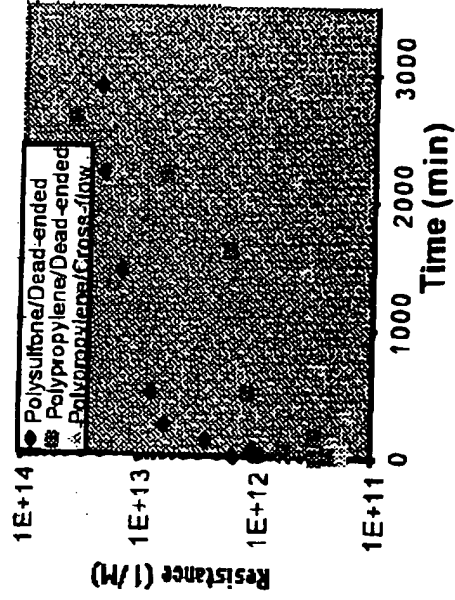
Flow Configuration



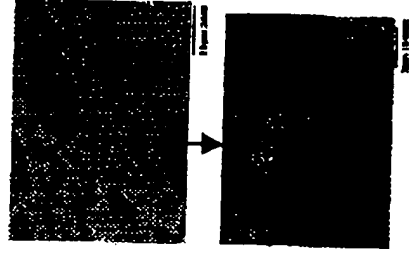
HepG2 Cells



STUDY OF FIBER AND FLOW TYPE



Polysulfone Dead-ended Flow



Polypropylene Dead-ended Flow

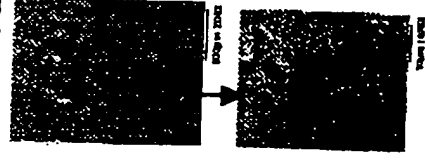
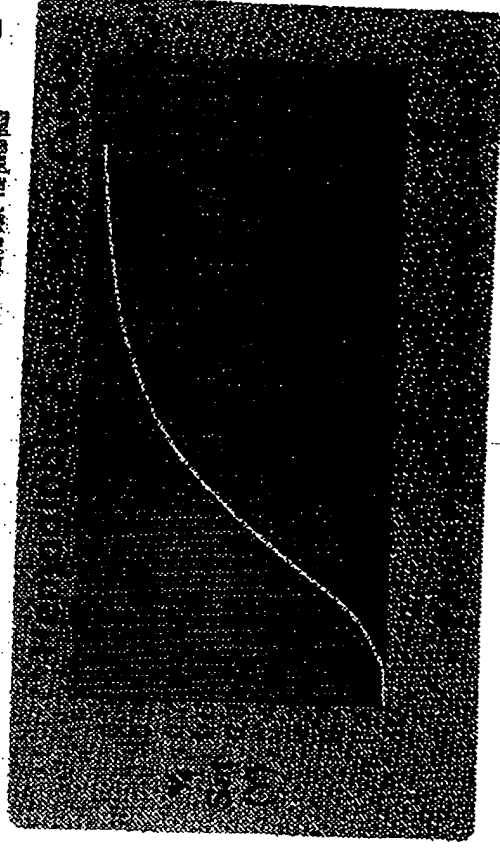
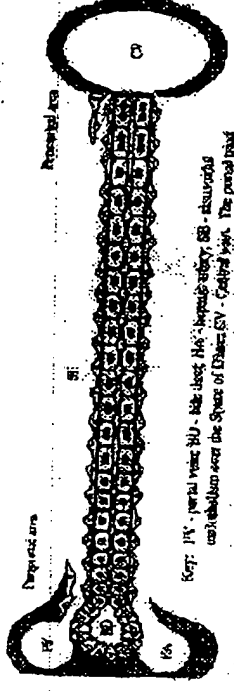


Figure 8

Effect of No Hemoglobin on Oxygen Mass Transfer (O_2 Gradients)

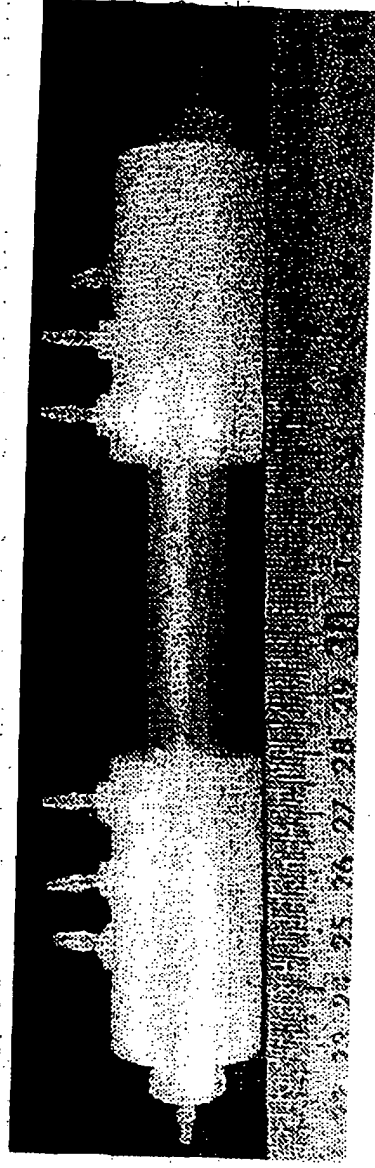
pO_2 (mmHg)	70	→	20
Hb-Bound	6.26 mM		2.91 mM
Free	0.1 mM		0.03 mM



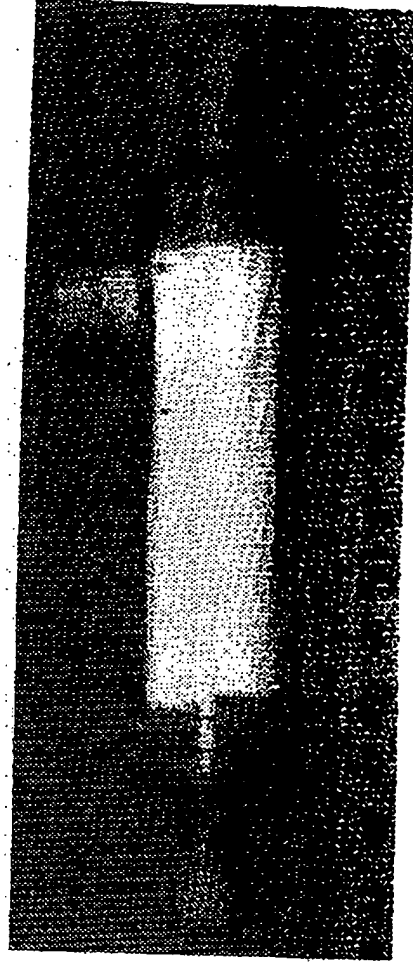
- Clotting factors - 'fouling'
- Perfluorinated hydrocarbons are peroxisome proliferators
- Synthetically modified hemoglobin blood substitutes that lack function: cooperativity.

Figure 9

Comparison of Conventional and Our Multicoaxial Bioreactor



Multicoaxial



Conventional

Figure 10

RESULTS

Hydrodynamic Model

Darcy's Law, $v = -K \nabla P$.

$$\Delta P = \frac{Q}{2\pi L} \left[\frac{\ln\left(\frac{r_b}{r_a}\right)}{K_1} - \frac{\ln\left(\frac{r_d}{r_c}\right)}{K_2} \right]$$

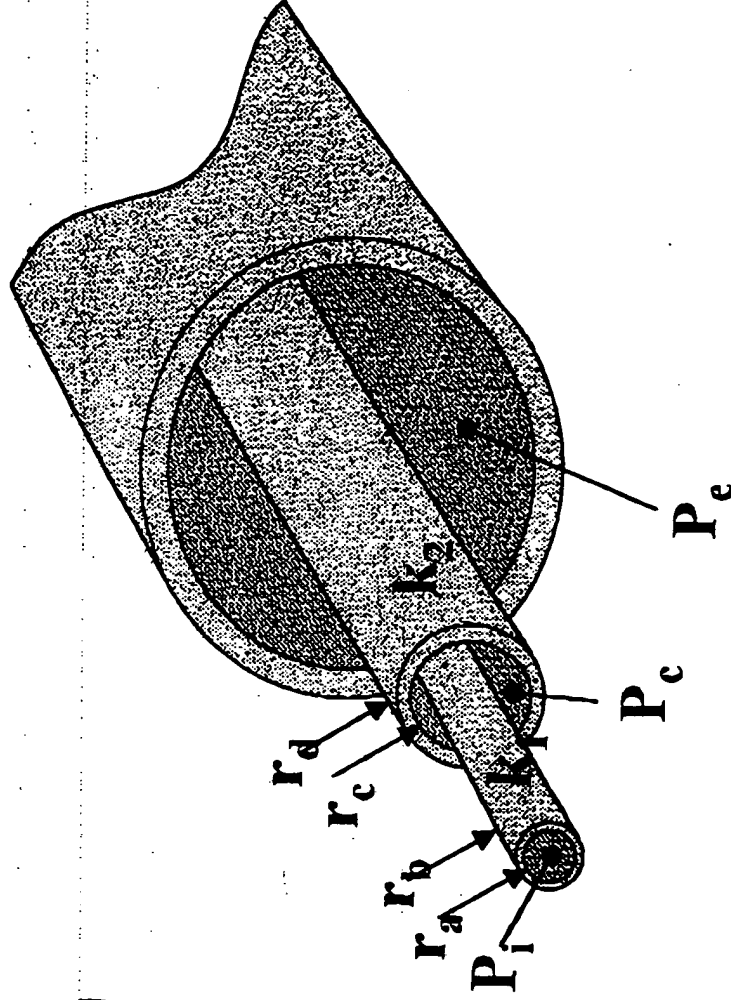
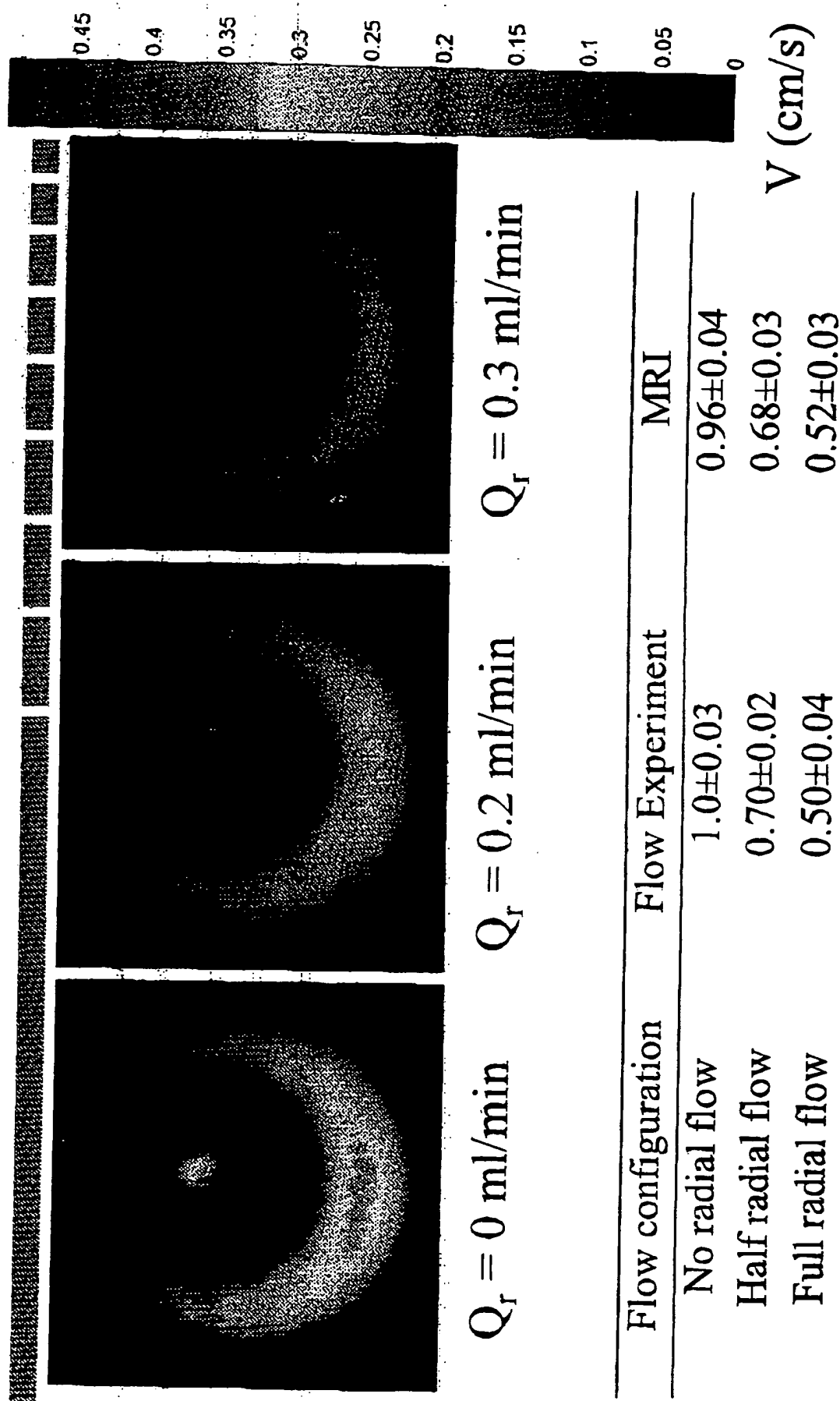


Figure 11

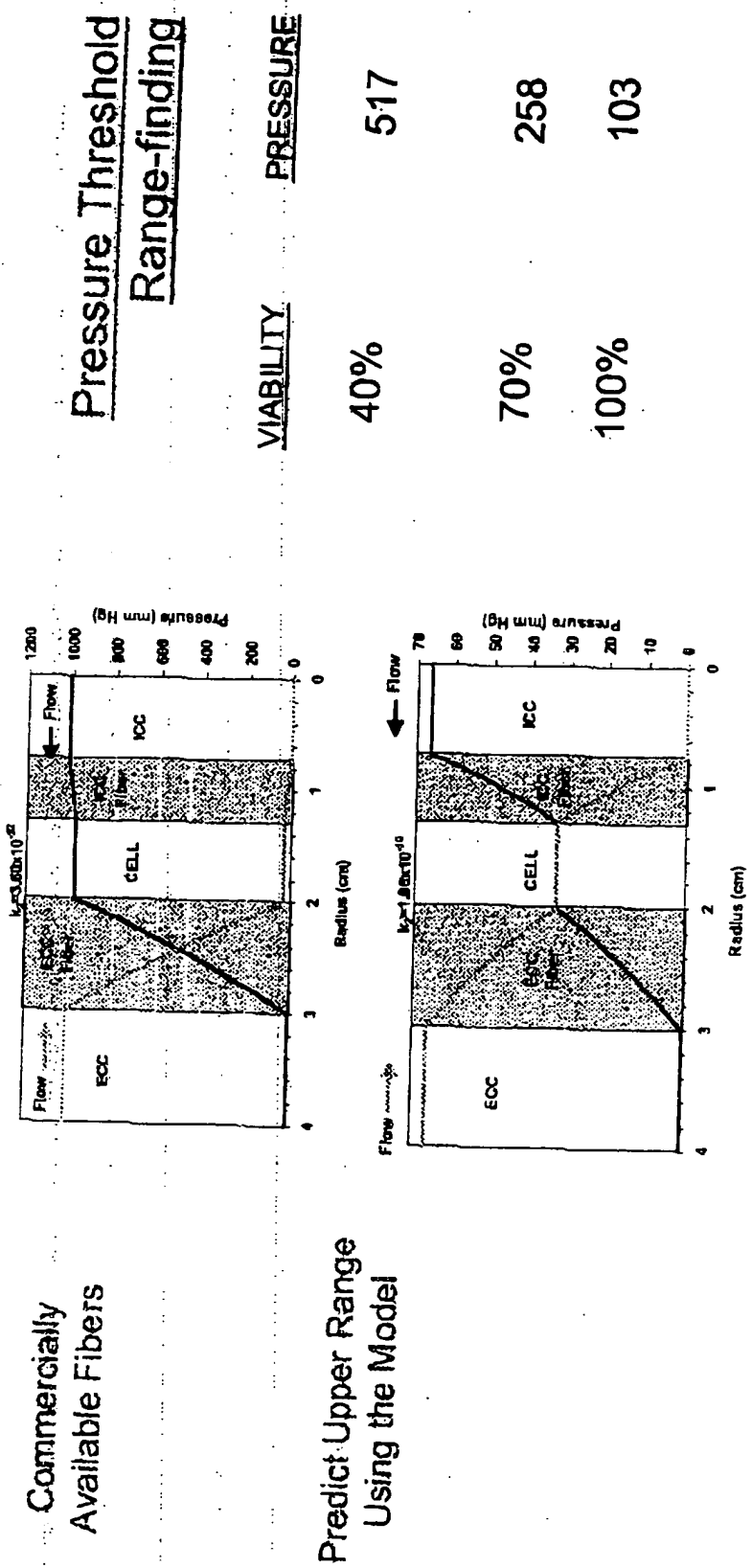
MRI used to determine axial flow



Flow configuration	Flow Experiment	MRI
No radial flow	1.0 ± 0.03	0.96 ± 0.04
Half radial flow	0.70 ± 0.02	0.68 ± 0.03
Full radial flow	0.50 ± 0.04	0.52 ± 0.03

Figure 12

Predicted Pressure Profile and Optimum K_1 and K_2



Average Pressure in Sinusoid = 5-10 mm Hg
 Average Sinusoidal Blood Flow = 0.01 cm/sec

Figure 13

Membrane 'Fouling' and Adverse Effect on Mass Transfer

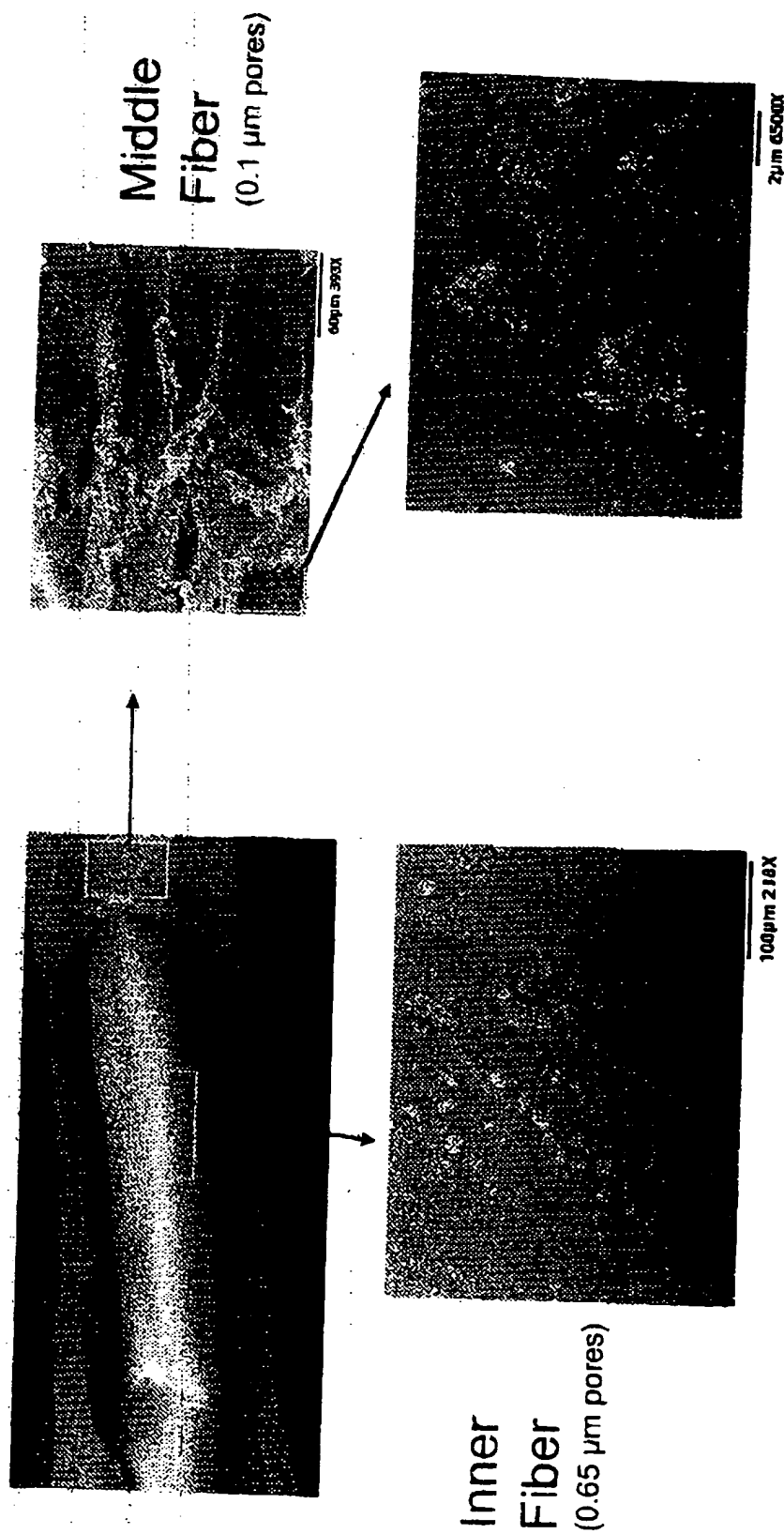
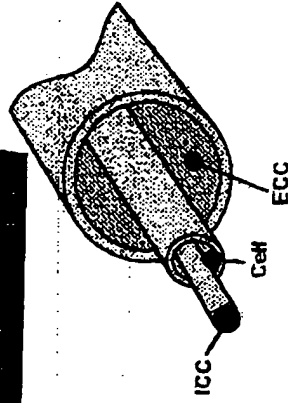
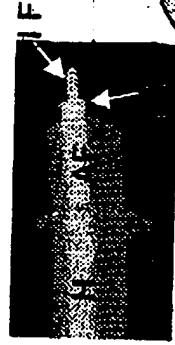


Figure 14

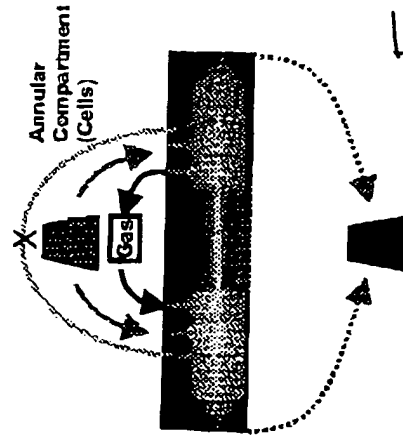
Dead-end and Cross Flow Configurations

Configurations for the Fouling Study

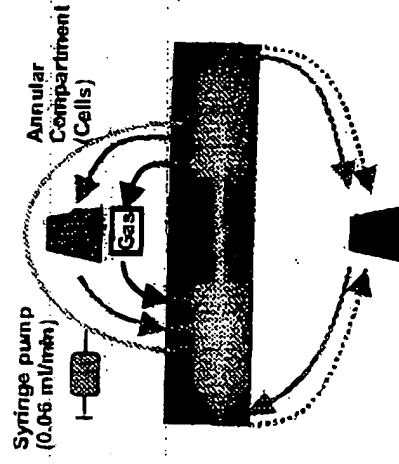
Multicoaxial Bioreactor



Dead-ended Flow Configuration



Direct Dead-ended Flow Configuration



Cross Flow Configuration

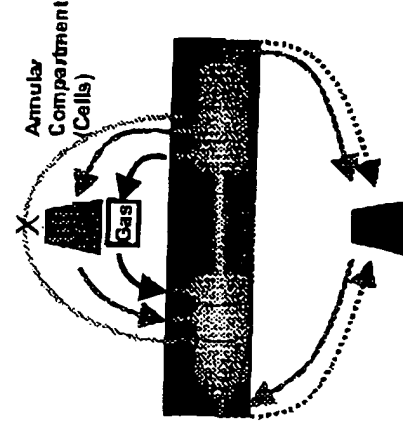


Figure 15

Results of the Dead-end and Cross Flow

Configurations for the Fouling Study

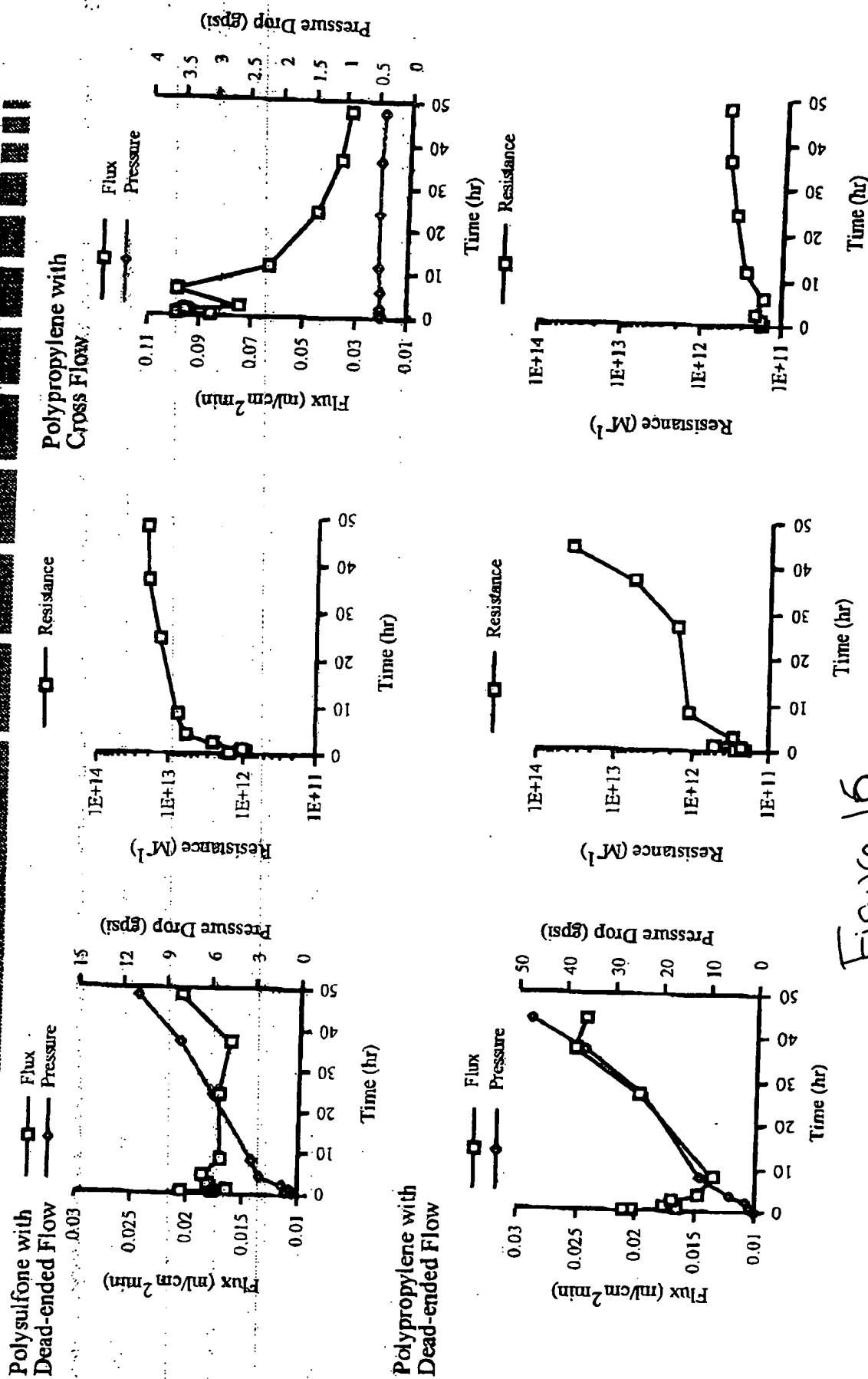
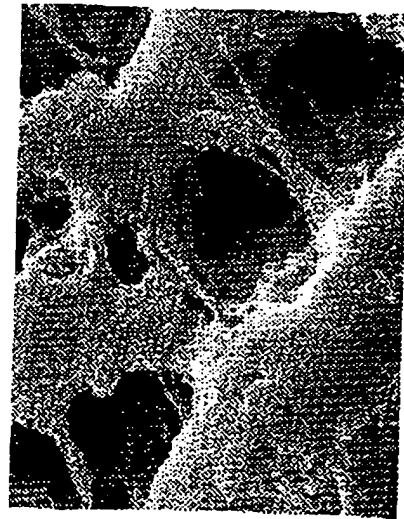


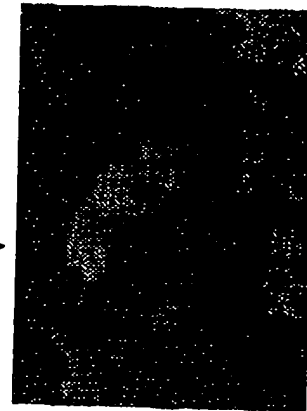
Figure 16

Results of the Dead-end and Cross Flow Configurations for the Fouling Study

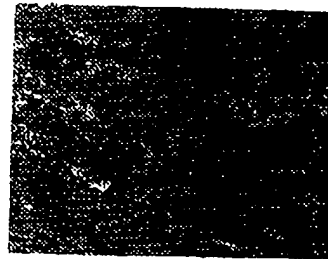
Clean polypropylene hollow fiber



Polysulfone + D-E



Polypropylene+ D-E



Polypropylene + Cross-flow

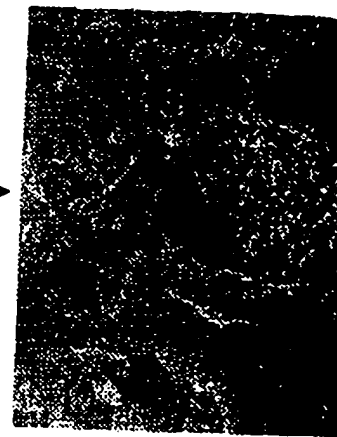
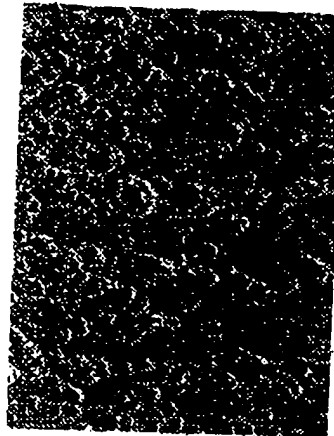
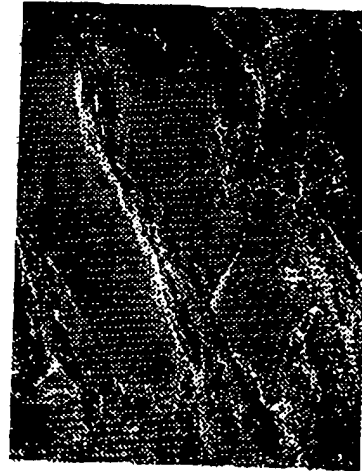
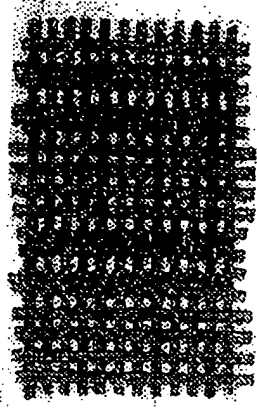
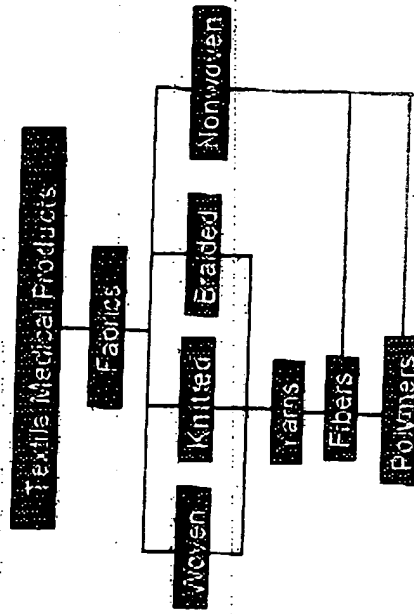
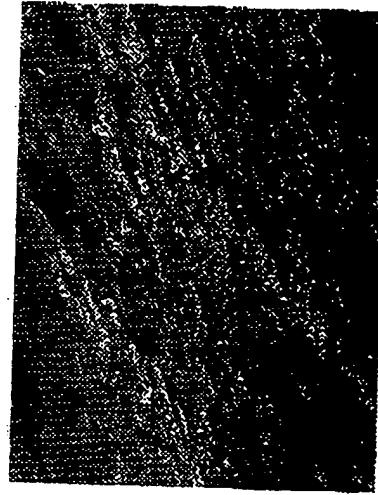


Figure 17

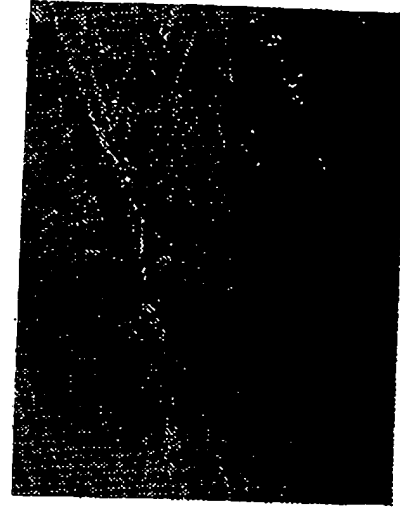
Fouling Studies of Woven Vasculature Incorporated into Multicoaxial Bioreactors



1mm 18X



1mm 22X



100µm 182X

Figure 17